

-continued

<210> SEQ ID NO 45
 <211> LENGTH: 24
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 45

Met Pro Arg Leu Phe Phe Phe His Leu Leu Gly Val Cys Leu Leu Leu
 1 5 10 15
 Asn Gln Phe Ser Arg Ala Val Ala
 20

What is claimed is:

1. A method of treating a human subject having a fibrotic disorder, comprising administering to said human subject an effective amount of a biologically active modified relaxin polypeptide, wherein: (a) said modified relaxin polypeptide comprises a relaxin A chain polypeptide and a relaxin B chain polypeptide, wherein said relaxin A chain polypeptide has a sequence at least 95% identical to SEQ ID NO: 4, and said relaxin B chain polypeptide has a sequence at least 95% identical to SEQ ID NO: 5 or SEQ ID NO: 6, and said non-naturally encoded amino acid is substituted in said A chain polypeptide at residue 1; and (b) said non-naturally encoded amino acid is linked to a linker or polymer, wherein said non-naturally encoded amino acid comprises a first functional group and the linker or polymer comprises a second functional group, wherein the first functional group and second functional group are not identical and each comprise a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group, and the resultant covalent linkage created by the reaction of the first and second functional groups comprises a triazole or an oxime linkage.

2. The method of claim 1, wherein the non-naturally encoded amino acid is selected from a para-substituted, ortho-substituted, or meta-substituted phenylalanine comprising a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group, or wherein said non-naturally encoded amino acid comprises para-acetyl-L-phenylalanine.

3. The method of claim 1, wherein the modified relaxin polypeptide exhibits an increased in vivo half-life by at least 2-fold relative to the human relaxin polypeptide of SEQ ID NO: 4 and SEQ ID NO: 5.

4. The method of claim 1, wherein said non-naturally encoded amino acid is linked to a linker and said linker is linked to a polymer, a water-soluble polymer, a polymer comprising poly(ethylene glycol), a label, a dye, a fatty acid, a carbohydrate, a saccharide, a cyclodextrin, a fluorophore, or biotin.

5. The method of claim 1, wherein said relaxin A chain polypeptide has the sequence of SEQ ID NO: 4 containing said substitution of said non-naturally occurring amino acid at residue 1 and said relaxin B chain polypeptide has the sequence of SEQ ID NO: 5 or SEQ ID NO: 6.

6. The method of claim 1, wherein the fibrotic disorder is selected from cardiac fibrosis, pulmonary fibrosis, renal fibrosis, hepatic fibrosis, coronary fibrosis, bone marrow fibrosis, dermatological fibrosis, and a fibrotic eye disorder.

7. A method of treating heart failure in a human subject in need thereof, comprising administering to said human subject an effective amount of a biologically active modified relaxin polypeptide, wherein: (a) the relaxin polypeptide

15 comprises a relaxin A chain polypeptide and a relaxin B chain polypeptide, wherein said relaxin A chain polypeptide has a sequence at least 95% identical to SEQ ID NO: 4, and said relaxin B chain polypeptide has a sequence at least 95% identical to SEQ ID NO: 5 or SEQ ID NO: 6, and said non-naturally encoded amino acid is substituted in said A chain polypeptide at residue 1; and (b) said non-naturally encoded amino acid is linked to a linker or polymer by a triazole or an oxime linkage.

8. The method of claim 7, wherein said non-naturally encoded amino acid is linked to said linker or polymer by an oxime linkage resulting from a reaction of a first functional group and a second functional group, wherein said first functional group comprises a carbonyl group and said second functional group comprises an aminooxy group.

9. The method of claim 8, wherein said non-naturally encoded amino acid comprises said first functional group and said second functional group is linked to said linker or polymer, and the oxime linkage resulting from the reaction of said first functional group and said second functional group links said non-naturally encoded amino acid to said linker or polymer.

10. The method of claim 7, wherein the non-naturally encoded amino acid is selected from a para-substituted, ortho-substituted, or meta-substituted phenylalanine comprising a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group, or wherein said non-naturally encoded amino acid comprises para-acetyl-L-phenylalanine.

11. The method of claim 7, wherein the modified relaxin polypeptide exhibits an increased in vivo half-life by at least 2-fold relative to the human relaxin polypeptide of SEQ ID NO: 4 and SEQ ID NO: 5.

12. The method of claim 7, wherein said non-naturally encoded amino acid is linked to a linker and said linker is linked to a polymer, a water-soluble polymer, a polymer comprising poly(ethylene glycol), a label, a dye, a fatty acid, a carbohydrate, a saccharide, a cyclodextrin, a fluorophore, or biotin.

13. The method of claim 7, wherein the heart failure comprises congestive heart failure.

14. The method of claim 7, wherein the heart failure comprises chronic heart failure.

15. The method of claim 7, wherein the heart failure comprises acute heart failure.

16. A method of treating heart failure in a human subject in need thereof, comprising administering to said human subject an effective amount of a biologically active modified relaxin polypeptide, wherein: (a) the relaxin polypeptide comprises a relaxin A chain polypeptide and a relaxin B chain polypeptide, wherein said relaxin A chain polypeptide comprises the amino acid sequence of SEQ ID NO: 4